

What is claimed is:

1. A method of therapeutically downmodulating an autoimmune response in a subject comprising administering an antigen binding portion of an anti-CD28 antibody that blocks signaling via CD28 to the subject such that an autoimmune response in the subject is downmodulated.
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2. The method of claim 1, wherein the antigen binding portion is an scFv molecule or an Fab fragment.
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3. The method of claim 1, wherein the antigen binding portion is humanized.
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4. The method of claim 1, wherein the antigen binding portion is fully human.
5. A method of therapeutically downmodulating an autoimmune response in a subject comprising administering a small molecule that specifically blocks signaling via CD28 to the subject such that an autoimmune response in the subject is downmodulated.
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6. The method of claim 1 or 5, wherein the autoimmune response is mediated by CD4+
20 T cells.
7. The method of claim 1 or 5, wherein the autoimmune response is mediated by CD8+
T cells.
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8. The method of claim 1 or 5, wherein the autoimmune response is type I diabetes.
9. A method of therapeutically downmodulating an ongoing autoimmune response in a subject comprising administering an antigen binding portion of an anti-CD28 antibody that blocks signaling via CD28 to the subject such that an ongoing autoimmune response in the
30 subject is downmodulated.

10. The method of claim 9, wherein the antigen binding portion is a scFv molecule or an Fab fragment.

11. The method of claim 9, wherein the antigen-binding portion is humanized.

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12. The method of claim 9, wherein the antigen-binding portion is fully human.

13. A method of therapeutically downmodulating an ongoing autoimmune response in a subject comprising administering a small molecule that specifically blocks signaling via

10 CD28 to the subject such that an ongoing autoimmune response in the subject is downmodulated.

14. The method of claim 9 or 13, wherein the autoimmune response is mediated by CD4+ T cells.

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15. The method of claim 9 or 13, wherein the autoimmune response is mediated by CD8+ T cells.

16. The method of claim 9 or 13, wherein the autoimmune response is type I diabetes.

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17. A method of prophylactically downmodulating an autoimmune response in a subject comprising administering an antigen binding portion of an anti-CD28 antibody that blocks signaling via CD28 to the subject such that an autoimmune response in the subject is downmodulated or delayed in its onset.

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18. The method of claim 17, wherein the antigen binding portion is a scFv molecule or an Fab fragment.

19. The method of claim 17, wherein the antigen-binding portion is humanized.

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20. The method of claim 17, wherein the antigen-binding portion is fully human.

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21. A method of prophylactically downmodulating an autoimmune response in a subject comprising administering a small molecule that specifically blocks signaling via CD28 to the subject such that an autoimmune response in the subject is downmodulated or delayed in its onset.

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22. The method of claim 17 or 21, wherein the autoimmune response is mediated by CD4+ T cells.

23. The method of claim 17 or 21, wherein the autoimmune response is mediated by
10 CD8+ T cells.

24. The method of claim 17 or 21, wherein the autoimmune response is type I diabetes.